0139

Use of B-lymphocyte (CD19+) Count as a Guide to Adjust the Doses of Rituximab Infusion in Paediatric Patients

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Introduction: Rituximab is a chimeric murine /human monoclonal antibody which has emerged as a novel therapy for various glomerular diseases in Children. The optimal doses remain uncertain. We presented our experience by monitoring the B-lymphocyte (CD19+) subset count as a guide to adjust the dose of rituximab infusion. This indicator helps to avoid over-immunosuppression and to optimize the duration of B-lymphocyte (CD19+) depletion.
Case Summaries: Patient 1: A 10-year-old boy had been diagnosed with steroid-dependent nephrotic syndrome since 2 years of age and was resistant to cyclophosphamide therapy. His nephrotic syndrome remitted with cyclosporin A but with frequent relapses. Renal biopsy confirmed focal segmental glomerulosclerosis. He had serious complications of steroid and became tacrolimus dependent. Two doses of rituximab infusion (375 mg/m^2) were given weekly. Depletion of B-lymphocyte (CD19+) was achieved after the 2nd dose of rituximab. His proteinuria improved and his steroid was weaned off 5 months after rituximab (Figure 1). Patient 2: A 16-year-old girl was diagnosed with systemic lupus erythematosus at 6 years of age. She had class III lupus nephritis diagnosed at 11 years old and was given a course of oral cyclophosphamide, followed by maintenance azathioprine and prednisolone. Mycophenolate mofetil and tacrolimus were added for recurrent relapses and uncontrolled disease. Two doses of rituximab infusion 500 mg (375 mg/m^2) were given weekly. She achieved better disease control with B-lymphocyte (CD19+) depletion which lasted for 4 months. Prednisolone was tapered to 7 mg daily. She experienced another relapse with nephrotic range proteinuria 9 months later. Another two doses of rituximab were given with good response. B-lymphocyte (CD19+) depletion lasted for another 10 weeks (Figure 2) and her prednisolone was reduced to 5 mg daily.

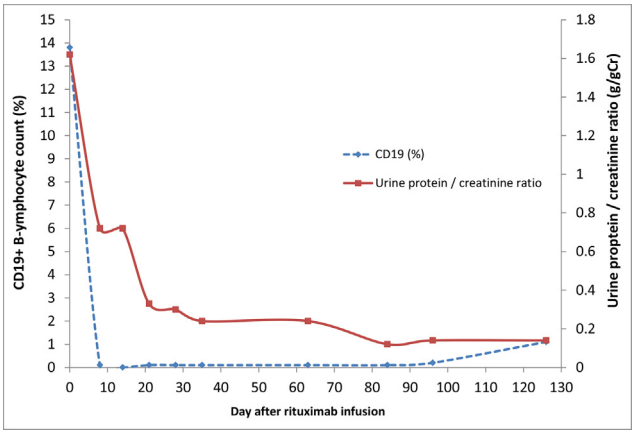

Figure 1. CD19+ count and urine protein / creatinine ratio after rituximab infusion of patient 1.

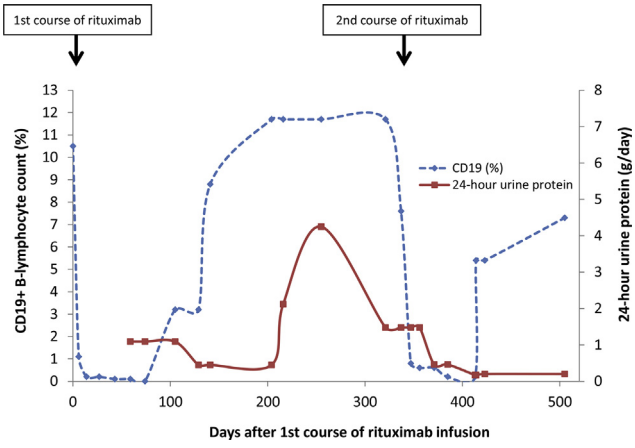

Figure 2: CD19+ count and urine protein / creatinine ratio after rituximab infusion of patient 2.

Conclusion: Two doses of rituximab can successfully deplete B-lymphocyte (CD19+). Monitoring of B-lymphocyte (CD19+) counts helps to adjust the dose of rituximab so as to prolong the duration of lymphocyte subset depletion.

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0147

"Late" is the Most Prominent Feature and Risk Factor for Patients with Late-onset Lupus Nephritis

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Objective: To distinguish the clinical and pathological characteristic of late-onset lupus nephritis (LN) patients and their prognosis.
Methods: This is a retrospective cohort study. Patients who were diagnosed as LN with age $\geq$ 14 from January 1st 1996 to December 31st 2011 were enrolled. Baseline clinical characteristics and pathological information were compared between late-onset group (LG) (onset age of LN $\geq$ 50) and the control group (CG) (onset age of LN $<$ 50), while the patient survival and renal outcome (definded as serum creatinine doubled or ESRD) were followed-up.
Results: Totally, 1264 patients were enrolled, with102 cases in LG and 1162 cases in CG. (1) The male to female ratio of LG was 2:5, doubling to the CG ($P = 0.001$). Patients in LG had more complications, higher systolic blood pressure and worse renal function (median eGFR: 59.59 vs 104.9 ml/min, $P < 0.001$). Patients with late-onset LN had a higher incidence of AKI (27.5% vs 16.5%, $P = 0.005$). No difference was shown on activity index of SLE between the two groups. The renal pathological comparisons indicated that chronic lesions of the LG were much more conspicuous than the CG, while the activity lesions of LN in two groups were similar. (2) During the follow-up time of 55 (1, 207) months, 291 patients reached the end-point, including 114 (13.1%) deaths, 107 (12.2%) creatinine doubled, and 80 (9.1%) ESRD. Kaplan-Meier curves showed that 5-year and 10-year survival rates of LG were 68.5% and 49.1%, respectively, much lower than that of the CG ($P < 0.001$). Patients in the LG had a worse renal survival compared to CG (log rank = 0.849, $P = 0.008$). The older onset-age was an independent risk factor for LN patients survival after adjusted for confounders (HR = 3.034, $P = 0.005$). Increased Scr at baseline was independently associated with renal survival while 1.1 mg/dL-increment of Scr would lead to the hazard ratio of renal disfunction increasing by 45% ($P < 0.001$).
Conclusion: The worse renal outcome of late-onset LN patients was more likely to be associated with the decline renal function with aging than the activity of SLE itself.

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0155

Clinicopathological Characteristics and Outcomes in Male Patients with Lupus Nephritis

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Objective: Long-term outcome of lupus nephritis (LN) in male patients is a controversial issue. The objective is to evaluate clinicopathological characteristics as well as renal and patient survival in male patients with lupus nephritis.
Methods: All patients who fulfilled American College of Rheumatology lupus Criteria were enrolled in the study. Clinicalpathological data of lupus nephritis patients with different gender were retrospectively analyzed and compared. Kaplan-Meier analysis and the Cox proportional hazards models were used to evaluate the risk factors associated with renal and patient survival in male lupus nephritis patients.
Results: A total of 1272 lupus nephritis patients were enrolled, with a mean age of 31.3 $\pm$ 13.4 years. Among them, 215 were male and 1057 were female. Clinical presentation was similar except that males had a significantly lower proportion of alopecia, arthralgia and leucocytopenia,

but tended to present a higher prevalence of fever, acute kidney injury, oliguria or anuria. During a median follow-up of 55.0 months, 107 (12.2%) patients had doubling of serum creatinine or ESRD (male 7.9% vs female 8.5%) and 114 (13.0%) patients died (male 14.9% vs female 7.8%). Regarding patient survival, compared with female patients, males had no difference in renal outcome but had significantly higher mortality than females.
Conclusion: The male lupus nephritis patients had worse renal function compared with female patients. Moreover, male patients had significantly higher mortality.

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0157
The Role of Interaction Between Renal Proximal Tubular Epithelial Cells and T Lymphocytes in the Pathogenesis of Tubulointerstial Inflammation in Lupus Nephritis

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Background: Renal proximal tubular epithelial cells (PTEC) and T lymphocytes assume pathogenic roles in tubulointerstitial inflammation in lupus nephritis (LN). Their interaction in such inflammatory process remains unclear.
Methods: CD4+ and CD8+ T cells were isolated from LN patients with (Group I) or without (Group II) moderate to severe tubulointerstitial inflammation, and co-incubated with PTEC in a transwell system. The level of cytokines in the culture media were measured after 72 hours of co-culture and compared between Group I and II patients.
Results: Twelve proliferative LN patients with (Group I; $n = 7$) or without (Group II; $n = 5$) moderate to severe tubulointerstitial inflammation were included. Group I patients showed significantly higher levels of RANTES ($p = 0.002$, 0.015 and 0.014) but lower IL-10 ($p = 0.018$, 0.015 and 0.022) when PTEC were co-cultured with their CD4+ T cells, CD8+ T cells or with both CD4+ and CD8+ T cells. Group I also demonstrated higher levels of MCP-1 ($p = 0.016$ and 0.042) when PTEC were co-cultured with their CD8+ T cells or with both CD4+ and CD8+ T cells. There is no statistically significant difference in IL-6 or IL-8, although Group I showed numerically much higher IL-6 levels.
Conclusion: A significant increase in RANTES and MCP-1 and a decrease in IL-10 levels were observed upon PTEC/T cell interaction in LN patients with moderate to severe tubulointerstitial inflammation, and hence suggest the putative roles of these cytokines in mediating tubulointerstitial inflammation in LN.

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0158
Risk Factors of Renal Relapse in the Era of Effective Immunosuppressive Treatments Among Chinese Lupus Nephritis Patients

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Objective: Repeated renal flares jeopardize the long-term kidney function in lupus nephritis (LN) patients. This study investigated the risk factors for relapse in the era of effective immunosuppressive treatments.
Methods: All LN patients who were followed up in Queen Mary Hospital during the period of 1 January 1983 to 31 December 2013 were reviewed. Episodes of renal relapses were identified and the risk factors for relapse were analyzed. The risk of relapse was also analyzed according to the era before (1983—1997) and after (1998—2013) the availability of mycophenolic acid (MPA) treatment in our centre.
Results: A total of 346 episodes of renal flares occurred in 184 patients (mean follow-up duration 195.3 $\pm$ 94.4 months). Multivariate analysis showed that age (OR 0.97; 95% CI 0.943—0.998; $p = 0.038$), higher serum creatinine on presentation (OR 0.992; 95% CI 0.985—0.999; $P = 0.019$),use of mycophenolic acid (MPA) as maintenance treatment (OR 0.322; 95% CI 0.0109—0.953; $P = 0.041$) and achievement of complete remission after induction therapy (OR 0.394; 95% CI 0.175—0.886; $P = 0.024$) were factors associated with lower risk of renal relapse. The choice of induction therapy, proteinuria and serological parameters on presentation did not affect the risk of subsequent flares (all $P > 0.05$). Rates of renal relapse were 0.044 and 0.024 relapse per patient-year before and after the availability of MPA treatment ($P < 0.001$). Patients who received prednisolone and MPA maintenance showed better relapse-free survival those on prednisolone and azathioprine (AZA) (83% vs. 68%, 66% vs. 42% and 62% vs. 37% at 5, 10 and 15 years; $P = 0.048$).
Conclusion: The risk of renal flare was low in the era of effective immunosuppressive treatments. The use of MPA as maintenance treatment might have contributed to lower risk of LN relapse and appeared to be more effective than AZA to prevent flares.

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0168
Variation and Clinical Significance of Circulation Annexin II in Patients with Systemic Lupus Erythematosus

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Objective: To compare the level of annexin II in patients with systemic lupus erythematosus, diabetic nephropathy, chronic glomerulonephritis and in normal control group, to explore the significance of the annexin II in systemic lupus erythematosus.
Methods: Thirty-five cases of patients with systemic lupus erythematosus, 10 cases of patients with diabetic nephropathy, and 10 cases of patients with chronic glomerulonephritis were enrolled in this study; 20 cases of healthy controls were also enrolled. Circulating annexin II in white blood cells was detected by flow cytometry. Student's t test, variance analysis and linear correlation analysis were used for statistics.
Results: Compared with healthy control cases, the level of annexin II in white blood cells in SLE patients (7.10 $\pm$ 2.89%) and DN patients (7.95 $\pm$ 3.72%) were significantly lower than that in healthy controls ($P < 0.01$, $P < 0.05$). In the SLE group, the level of annexin II in patients who were more active (SLEDAI $\geq$ 9) decreased more than in those who were less active (SLEDAI < 9; $P < 0.05$). As for annexin II, a positive correlation was found with serum albumin ($r = 0.439$, $p < 0.01$), negtive correlation was found with urine protein/urine creatinine ($r = -0.382$, $p < 0.05$), SLEDAI ($r = -0.417$, $p < 0.05$), and D-dimer ($r = -0.336$, $p < 0.05$).
Conclusion: The level of annexin II is decreased in patients with systemic lupus erythematosus. It can be used as a reflection of the abnormality of the coagulation and fibrinolytic systems. It may be used as a good indicator of the prothrombotic state in SLE patients, and be helpful in judging the activity and therapeutic effect of the disease.

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0192
Effect of Rituximab on Serum Levels of Anti-C1q Antibodies and Antineutrophil Cytoplasmic Autoantibodies in Refractory Severe Lupus Nephritis

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Objectives: To analyze and compare the effects of rituximab (RTX) and cyclophosphamide (CTX) on the serum levels of anti-C1q antibodies and